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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/547,843	09/06/2005	Takashi Horiguchi	Q101074	9679

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/547,843	HORIGUCHI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-7 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 06, 2008 has been entered.

Response to Amendment

2. Claims 1, 2, 4 and 6 have been amended and claims 10 and 26 have been cancelled as requested in the amendment filed on March 06, 2008. Following the amendment, claims 1, 2, 4-7 and 17 are pending in the instant application.

Claims 1, 2, 4-7 and 17 are under examination in the instant office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on March 06, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1, 2, 4-7 and 17 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility for reasons of record in section 5 of Paper mailed on May 11, 2007 and in section 5 of Paper mailed on October 10, 2007.

At pp. 4-5 of the Response, Applicant argues that the instant specification specifically addresses the scientific background that supports the working hypothesis of the instant invention, "[t]he relation between cell death and β-amyloid secretion disclosed in the Example and neurodegenerative diseases such as Alzheimer's disease is taught in the BACKGROUND ART section of the present specification. Specifically, it is taught that (A) if a Pael receptor has abnormality (such as an incomplete higher-order structure), it is usually rapidly decomposed by the action of Parkin, but when the proteolysis system is suppressed, abnormal Pael receptors are accumulated in endoplasmic reticula, and the cell falls into cell-death due to endoplasmic reticulum stress (Cell, 105:891-902 (2001)); and (B) production of β-amyloid is increased due to lack of Irel participating in endoplasmic reticulum stress response (Biochem. Biophys. Acta., 1536:85-96 (2001); and J. Biol. Chem., 276:2108,2114 (2001)) (see page 1, line 25 to page 2, line 4)". Applicant further argues that "[t]hose skilled in the art would understand from the specification, as discussed above, and by Examples 4 and 5, that inhibition of the expression of C 1 results in inhibition of cell death and an increase in the secretion of β-amyloids, and thus it would be effective for treating Alzheimer's disease, Parkinson's disease and the like. Thus, it would be reasonable that compounds that inhibit the expression (or the activity) of C 1 can be used for treating neurodegenerative disease such as Alzheimer's disease" (bottom at p. 5).

Applicant's arguments have been given careful consideration but are not found to be persuasive for the following reasons.

As fully explained in the previous communications of record, the instant claims are drawn to an isolated nucleic acid molecule and the protein encoded thereby of as yet undetermined function or biological significance. Specifically, the present invention relates to "a prophylactic/therapeutic agent for a neurodegenerative disease, [and] a β-amyloid production inhibitor" (p. 1 of the specification), and is based on the hypothesis that "a target gene for creating a medicine for neurodegenerative diseases can be found in genes participating in endoplasmic reticulum stress response" (p. 2 of the specification). The instant specification asserts that "[t]he protein of the present invention regulates repair and decomposition of abnormal proteins, neuronal death, amyloid production, etc. because its expression is increased upon application of endoplasmic reticulum stress to nerve cells" (p. 30). The instant specification does not disclose biological role of C1 protein of SEQ ID NO: 1, its relevance to any specific physiological process or clinical condition, and fails to provide any scientific reasoning to support a statement that genes "participating in endoplasmic reticulum stress response" have a specific significance during neurodegeneration.

Example 4, p. 69 of the instant specification demonstrates that cells transfected with C1 gene had increased survival rate as compared to control cells (see Figures 1 and 2). The specification does not disclose any scientific reasoning as how this data support the role of C1 protein in Alzheimer's disease. Further, Example 5, p. 69 of the instant specification describes results of experiments, in which cells transformed with C1 gene were recorded to secrete less Aβ than control cells. However, there is no explanation given as how spontaneous secretion of Aβ in

cells transfected with C1 relates to etiology of Alzheimer's disease in particular, even more for Parkinson's disease, in which amyloid pathology seems not to be present, and to neurodegenerative diseases in general.

According to the knowledge in the art, neurodegenerative diseases are heterogeneous in etiology, symptomology and epidemiology. At p. 5 pf the Response, Applicant states that, "C 1 [...] would be effective for treating Alzheimer's disease, Parkinson's disease and the like". However, the art recognizes that only a few neurodegenerative diseases, Alzheimer's disease included, have amyloid (Aβ) as a recognized pathological factor. The instant specification fails to provide any factual evidence or a line of scientific reasoning to support a conclusion that a protein, of which no biological role or relevance to a specific physiological process or clinical condition is known, has a specific physiological role, such as inhibition of β-amyloid production or inhibition of cell death in general and thus causative during neurodegeneration.

The Declaration of Tomomichi Watanabi under 37 CFR 1.132 filed on March 06, 2008 is insufficient to overcome the rejection of claims 1, 2, 4-7 and 17 based upon 35 U.S.C. 101 as set forth in the last Office action because it is limited to presenting additional data obtained on cells transfected with C1 protein and studied for cell death promotion activity and secretion of Aβ. As an essential matter, the validity of the data is not and has never been disputed by the Examiner. However, as it was pointed out in previous office actions of record, the experimental data of record or scientific articles cited previously and with the instant Response of March 06, 2008, fail to address the significance of the experimental model used by Applicant with respect to Alzheimer's disease, for example, or to provide any support or further explained the relevance of findings presented in the instant specification to neurodegenerative pathology of the brain.

The Court in *Brenner v. Manson* held that "[t]he basic *pro quid quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point – where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

§101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form *Brenner*, 383, U.S. at 534-35, 148 USPQ at 695. *Brenner's* standard has been interpreted to mean that "vague, general disclosures or arguments of "useful in research" or "useful as building blocks of value to the researcher" would not satisfy §101. See *Kirk*, 376 F. 2d at 945 153 USPQ at 55 (interpreting *Brenner*).

Characterization of the claimed nucleic acids of SEQ ID NO: 2 and encoded protein of SEQ ID NO: 1as affecting secretion of Aβ or survival of cells artificially transfected with the protein is clearly not sufficient to establish their utility. The art does not recognize the cell model used in the experiments disclosed in the instant specification as acceptable for "Alzheimer's disease, Parkinson's disease and the like". The Examiner does not dispute the experimental data presented by Applicant; however, the issue at hand remains that in the absence of knowledge of the biological significance or activity of these particular claimed nucleic acids and polypeptide and their relevance to the process of cell death or secretion of abnormal amyloid protein, the instant C1 is suitable only for future research. Applicant states at p. 5 of the Response that, "the present invention has a specific and substantial credible utility of screening for compounds that inhibit the activity of the protein of the present invention. The present invention has the specific

and substantial credible utility of screening for compounds that inhibit the expression of the protein", but the record does not support Applicant's position. Because the activity of the C1 protein is not known, one skilled in the art would not how to identify a compound that inhibits that activity and certainly would not reasonably expect such compound to have any effect on the course of Alzheimer's disease or any other neurodegenerative condition.

Thus, the record does not support Applicant's position that the characterization of a protein of SEQ ID NO: 1 as inhibiting Aβ secretion within an artificial model of cells overexpressing that protein would have suggested a specific biological function, or any other basis for patentable utility, to a person skilled in the art at the time the application was filed. In the terms used by the *Brenner* Court, such a characterization does not provide a specific utility in currently available form.

The specification provides no meaningful guidance regarding how to use such information in any practical way. The specification provides no guidance on how such information would allow those skilled in the art to use the claimed polynucleotides in a specific substantial way. Thus, Applicant claims a product asserted to be useful in screening compounds for future clinical applications but the specification does not disclose how to interpret those data.

The Examiner maintains that since the instant specification does not disclose a credible "real world" use for the encoded protein in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, 4-7 and 17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 17 is indefinite as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the elements that comprise the instant claimed kit. Claim 17, as presented, encompasses a kit for screening a compound or its salts that promotes or inhibits the activity of the protein [of SEQ ID NO: 1] and the only element that is recited in the kit is the protein itself. Since the activity of the protein of SEQ ID NO: 1 is not known (see reasons of record in section 6 of the instant office action), and because there appears to be no patentably significant utility in screening for compounds that affect the activity of the protein of SEQ ID NO: 1, one skilled in the art would now know as what material limitations define the claimed subject matter, a kit comprising protein of SEQ ID NO: 1.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

May 6, 2008

/Olga N. Chernyshev, Ph.D./
Primary Examiner, Art Unit 1649